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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/508,516	06/08/2000	CHRISTOPHER ROBERT BEBBINGTON	078883/0119	3014

7590 01/15/2002

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EXAMINER

WILSON, MICHAEL C

ART UNIT PAPER NUMBER

1633

19

DATE MAILED: 01/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory ActionApplication No.
09/508,516Applicant(s)
Bebbington et al.Examiner
Michael C. WilsonArt Unit
1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED Jan 2, 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY (check only a) or b)]

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☒ In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for the reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.
3. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search. (See NOTE below);
- (b) ☐ they raise the issue of new matter. (See NOTE below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: _____

4. ☒ Applicant's reply has overcome the following rejection(s):
112/2nd re: splice site "encoding"
5. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claim(s).
6. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
see attached
7. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
8. ☒ For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):
Claim(s) allowed: _____
Claim(s) objected to: _____
Claim(s) rejected: 1-19, 21-24, 30, and 42
9. ☐ The proposed drawing correction filed on _____ a) ☐ has b) ☐ has not been approved by the Examiner.
10. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
11. ☐ Other: _____

MICHAEL C. WILSON
PATENT EXAMINER
ART UNIT 1633

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Applicants argue the specification enables the claims by teaching other combinations of "NOI" are enabled because the skilled artisan was aware of cryptic splice donors/acceptors, could readily detect them and could readily eliminate them. Applicants argument is not persuasive. Sebillon, Maruyama, Reichel and Burn taught cryptic splice sites and mutating cryptic splice sites to improve expression. The references do not correlate to the claims because they do not teach how to activate splice sites upon transduction in a retroviral vector or teach how to use the mutated sequences in combination with other "NOI" as claimed.

Applicants argue the claims directed toward gene therapy have been canceled. Applicants argument is persuasive as it relates to claims 20, 25, 26, 28 and 43-45 which have been canceled. However, claim 5 recites a "therapeutic agent" which, based on the teachings of the specification, implies the product is capable of a therapeutic effect. Therefore, claim 5 remains rejected for reasons of record regarding *in vivo* embodiments for therapy.

Applicants argue the amendment to claim 1 clarifies the relationship between the retroviral vector and the pro-viral vector. Applicants argument is not persuasive because the proposed amendment to claim 1 clarifies the nucleotide sequences "contain" splice sites - not "encode" splice sites. The proposed amendment does not address the rejection regarding the relationship between the retroviral and pro-viral vectors in claim 1 or between claim 1 and dependent claims 4, 7, 8, 11 and 12. The proposed amendment would overcome the indefiniteness rejection regarding "encode". The claims remain rejected for reasons of record regarding the relationship between the retroviral and pro-viral vectors in claim 1 or between

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claim 1 and dependent claims 4, 7, 8, 11 and 12.

Applicants argue Morgenstern does not teach the splice donor sites in the positions claimed. Applicants argument is not persuasive. Morgenstern taught a retroviral vector and pro-viral vector having a splice donor site flanking the DNA encoding the protein of interest which is equivalent to the functional splice donor sites in claim 1. Claim 2 requires a the pro-viral vector have a "non-functional donor site" upstream of the splice acceptor site. The pro-viral vectors of Morgenstern have numerous sites upstream of the splice acceptor site that do not function as a donor site which is equivalent to claim 2. Claims 1-6, 9, 10, 12-14, 18, 19 and 21-24 remain rejected for reasons of record over Morgenstern.

Applicants argue Takada and Kriegler do not teach regions encoding splice donor sites within LTRs. Applicants argument is not persuasive because the claims do not require splice donor sites within LTRs. Claims 1 and 15-17 remain rejected for reasons of record over Takada. Claims 1 and 9-11 remain rejected for reasons of record over Kriegler.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of formal matters can be directed to the patent analyst, Tracey Johnson, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-2982.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael C. Wilson



MICHAEL C. WILSON
PATENT EXAMINER